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SAWAI SEIYAKU KK *J0 1075-421-A
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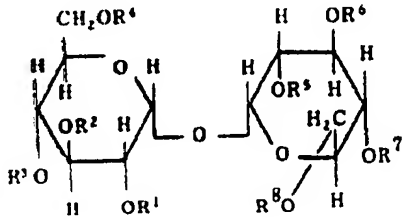
New freeze-dried liposome prepn. - contg. alpha, alpha-trehalose tri:mycolate and having immune-activating and antitumour-action

C89-058598

B(7-A2, 12-A1, 12-A6, 12-G7, 12-M11F)

Freeze-dry liposome prepns. contain α,α-trehalose trimycolate of formula (I)



(I)

R^1 - R^8 = H or mycolic acid residue, but three of them are mycolic acid residues and the others are H;

the mycolic acid residues may be the same or different.

MORE SPECIFICALLY

$R^1 = R^2 = R^8$ = mycolic acid residue, others = H (GL-2);
$R^1 = R^4 = R^8$ = mycolic acid residue, others = H (GL-1).

USE/ADVANTAGE

(I) is known to have immune-activating action and antitumour action with relatively low toxicity [PCT/JP87/00171]. (I), however, is insoluble or sparingly soluble in water or lower alcohol, so that (I) formulations are unstable and the activity of (I) is decreased.

The freeze-dry liposome formulations can be prepd. easily in stable form, which when dispersed into aq. medium can be reconstituted into liposomes at high rate.

The formulations may be for oral or parenteral (i.p., i.v. s.c.) admin., e.g. tablets, powder, pills, syrup, injection, suppositories, and administered in a single or in divided doses of 10 mg - 2 g, pref. 500 mg - 1 g, a day for an adult.

PREPARATION

The liposome is prepd. by dissolving (I) and phospholipid or phospholipid-contg. material (e.g. phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, phosphatidylserine) in an organic solvent and dispersing the resulting soln. into an aq. medium (e.g. water, physiological saline, buffer, sugar soln.).

The organic solvent includes $CHCl_3$, MeOH, and EtOH. The freeze-drying may be carried out at -20 to -50°C under reduced pressure of 0.1 Torr or lower.

EXAMPLE

A soln. of egg yolk phosphatidylcholine (15 μ mole) and GL-2 (1 mg) in $CHCl_3$ was placed in a round bottom flask and $CHCl_3$ was distilled off under reduced pressure at 25-30°C to form a thin film on the inside wall of the flask. A phosphate-buffered physiological saline (pH 7.0; 1 ml) was added and the mixt. was stirred until the film peeled off. The resulting liposome was frozen by dry-ice-MeOH and dried to give the liposome prepn.(9ppW52EDDwgNo0/6).